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Case Report

Multifactorial Neonatal Thrombosis in Inferior Vena Cava Dislodged to the Right Atrium: A Case Report

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ABSTRACT

***Background*:** Neonatal thrombotic diseases can cause mortality or serious morbidity and disability.
Case report: In this report, we present a case of neonatal inferior vena cava thromboembolism with several underlying factors. Hereditary thrombophilia and genetic mutation in plasminogen activator inhibitor-1 and *MTHFR A1298C* genes in conjunction with cleft palate resulted in poor lactation and hypernatremic dehydration. A peripherally inserted central catheter in the inferior vena cava was an additional underlying factor. Thrombosis mass was dislodged to the right atrium while asymptomatic and accidentally detected during routine echocardiography.
Conclusion: Surgical thrombectomy was done successfully, and the mass was removed from the right atrium.

Keywords: Hereditary thrombophilia, Hypernatremic dehydration, Neonatal thrombosis, Peripherally inserted central catheter

Introduction

Thrombotic diseases, either venous or arterial, can cause mortality or result in serious morbidity and disability (1). Ranges of neonatal thromboembolic events have varied from 2.4 clinically apparent events (excluding stroke) per 1000 neonatal intensive care unit (NICU) admissions (2) to 5.1 events per 100,000 live births (3). Neonatal thromboses occur in both preterm and term infants and affect male and female infants equally (3, 4).

Genetic mutation and hereditary thrombophilia is the most important cause of neonatal thrombosis (5). The occurrence of thrombosis could be grounded in the use of central vascular access with a high risk for mechanical, infectious, and thrombotic complications. The use of central lines is the most common cause of thrombosis in neonates and infants (6, 7). Other risk factors for thrombosis are asphyxia, septicemia, dehydration, and maternal diabetes (1).

Cleft lip and cleft palate are common birth defects, affecting about one baby per 700 births. Feeding these babies is an immediate concern, and there is evidence of delay in the growth of children with a cleft as compared to those without clefting. In an effort to combat reduced lactation (8), we present a rare case of neonatal thrombosis of inferior vena cava (IVC) dislodged to the right atrium. This condition was associated with several factors from hereditary thrombophilia to cleft palate and hypernatremic dehydration and finally successful thrombectomy.

Case report

The patient was a 10-day-old girl with a birth weight of 3,950 g, height of 53 cm, head circumference of 36 cm, and 1-min Apgar score of 9/10. She was born as the first child. In the initial examination, the cleft palate was observed. The baby was discharged after birth without admission or training of the mother about breastfeeding considerations.

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Table 1. Results of laboratory tests before admission

Tests		Results	Unit
Wight blood cells (WBC)	17,700	Neutrophils=55.9% Lymphocytes=37.1% Monocytes=6.9%	(*10^3 /µl)
Hemoglobin (Hb)		19.5	(g/dl)
Platelets(plt)		245	(*10^3 / µl)
Sodium (Na)		178	(meq/L)
Potassium (K)		6.1	(meq/L)
Blood urea nitrogen(BUN)		198	(mg/dl)
Creatinine (Cr)		2.7	(mg/dl)
Blood glucose (BS)		432	(mg/dl)
Ammoniac		64	(µmol /L)
Lactate		23	(mg/dl)
Pyruvate		1.5	(mg/dl)

Ten days after birth, the infant was referred to the hospital with irritability, poor feeding, lethargy, The baby had not fed milk well in the last 10 days. Mother had no problem with her pregnancy history and did not use any special medications. Parents had no consanguineous relations. In the initial examination, the infant was hypotonic with increased skin turgor. Blood pressure was 85/pulse, respiratory rate and heart rates were respectively 45 and 140 per minute, and O_2 saturation was 97% in pulse oximetry. Heart sound was normal, and she had no organomegaly. The weight at the time of admission was 3000 g. The results of initial laboratory tests are listed in Table 1.

Because of very high sodium and high levels of blood urea nitrogen (BUN) and creatinine (Cr), the initial diagnosis was dehydration due to poor feeding probably because of a large cleft palate. The patient was admitted, serum therapy started, and peritoneal dialysis was performed due to the lack of urine and high creatinine. She became isolated and frequent peritoneal culture was performed. A peripherally inserted a unilumen silicone central catheter (PICC) was embedded in IVC, and its correct position was confirmed. In the level of the diaphragm in the X-ray (Figure 1), high-pressure fluid was avoided, and blood transfusion was not used. The results of the repeated tests of sodium, potassium, BUN, and Cr in 6-7 consecutive checks every 4-6 h are presented in Table 2.

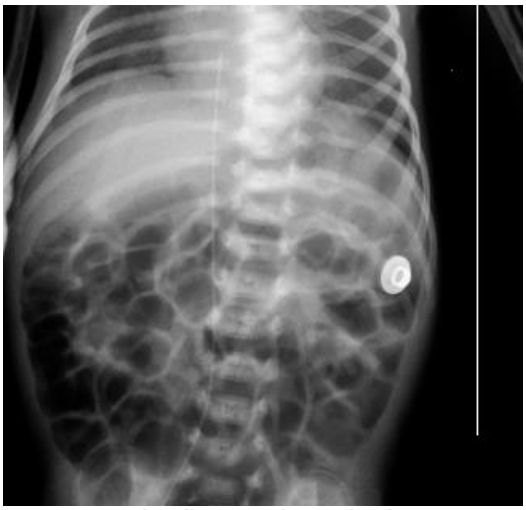


Figure 1. Peripherally inserted central catheter tip

The results of the C-reactive protein test and microbial cultures of blood, urine, peritoneal dialysis fluid, and cerebrospinal fluid were normal; therefore, there was no evidence of sepsis. The results of the brain and abdominal sonography were normal.

In routine echocardiography assessment, a great thrombosis was observed in the IVC (Figure 2). The baby was intubated on the same day because of severe respiratory distress. Hemoglobin suddenly dropped to 11.3 g/dl, and coagulation tests were disrupted. Prothrombin time was 16.2 sec, international normalized ratio was 1.42, and partial thromboplastin time

Table 2. Consecutive results of sodium, potassium, blood urea nitrogen, and creatinine tests

Test	Repeat						
	1	2	3	4	5	6	7
Sodium (meq/L)	178	174	169	168	166	160	152
Potassium (meq/L)	6.1	5. 3	3. 8	4. 3	4. 1	3.8	4.5
Blood urea nitrogen (mg/dl)	198	91	41	22	10	5	-
Creatinine (mg/dl)	2.7	1.8	1.2	1.1	0.7	0.6	-

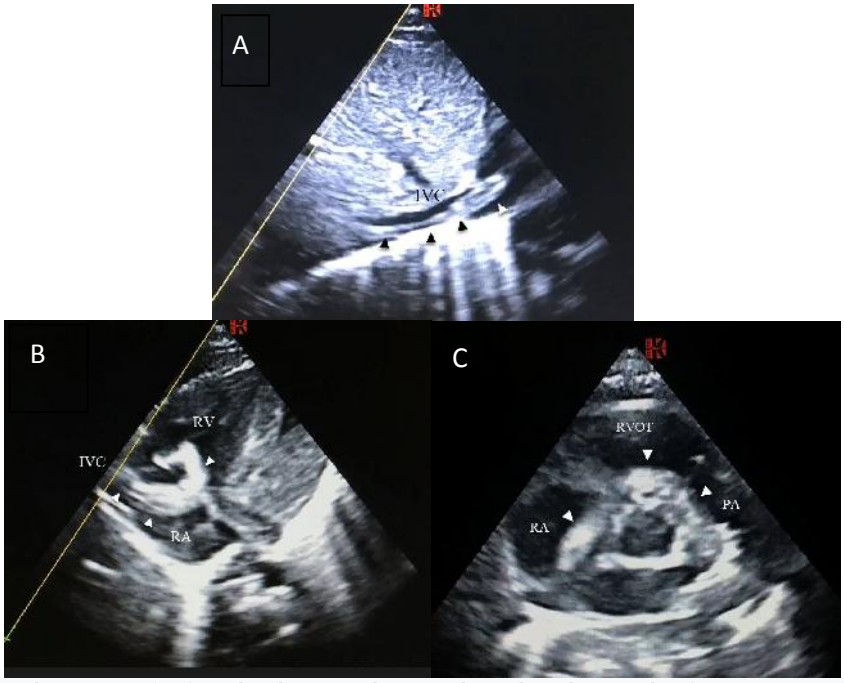


Figure 2. Echocardiographic images; A) a four-chamber view showing a large thrombosis with inferior vena cava (IVC) origin is crossing the tricuspid valve (arrowhead is showing thrombosis), B) short-axis view showing thrombosis in the right atrium (RA) which is propagated to the pulmonary artery, and C) a large thrombosis seen in IVC with propagation to RA

Table 3. Results of coagulation test

Tests	Results
Antiphospholipid antibody IgG	1.3 time
Antiphospholipid antibody IgM	1.4 time
Anti-RO (SS-A) antibody	Negative
Anti-LA (SS-B) antibody	Negative
Fluorescent antinuclear antibody(FANA)	Negative

was 30 sec. The primary results of the coagulation test were normal (Table 3).

Repeated echocardiography showed the origin of the clot was the suprahepatic part of IVC that spread to the right atrium and was dislodged to the mean pulmonary artery and right pulmonary artery.

After cardiovascular consultation, enoxaparin was advised but was not injected because of coagulation disorder and blood supply consultation. Heart surgery consultation was done on the same day, and thrombectomy was performed to remove thrombosis (Figure 3). The patient was discharged with anticoagulant and in good general condition 2 weeks after the surgery.

Because of the dislodgement of thrombosis, genetic tests were requested. The results of genetic tests to study the polymorphism in coagulation genes showed a mutation in plasminogen activator inhibitor 1 (*PAI-1*) and *MTHFR A1298C* genes, which indicated a hereditary thrombophilia (Figure 4).

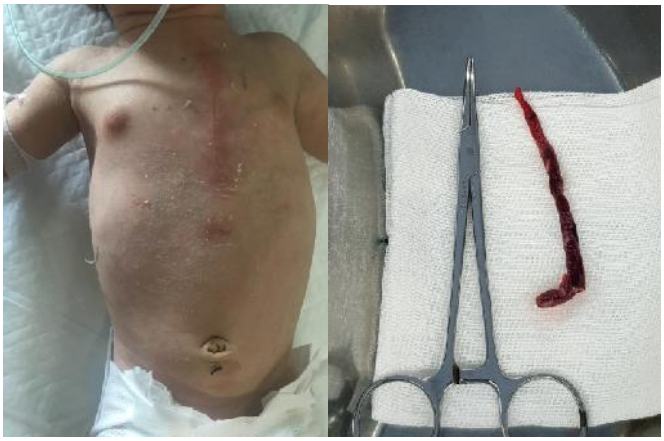
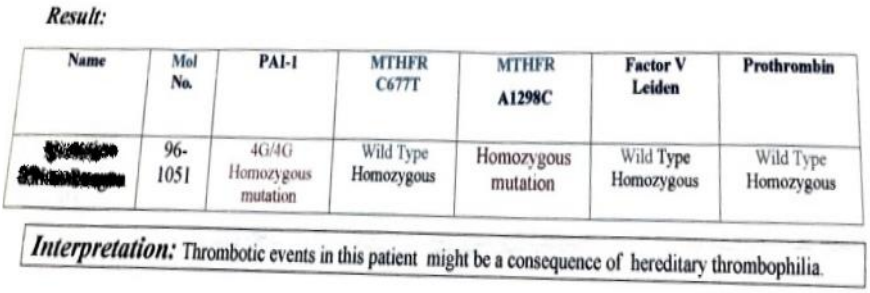


Figure 3. Thrombosis mass removed from inferior vena cava and right atrium



Result:

Name	Mol No.	PAI-1	MTHFR C677T	MTHFR A1298C	Factor V Leiden	Prothrombin
[redacted]	96-1051	4G/4G Homozygous mutation	Wild Type Homozygous	Homozygous mutation	Wild Type Homozygous	Wild Type Homozygous

Interpretation: Thrombotic events in this patient might be a consequence of hereditary thrombophilia.

Figure 4. Results of genetic tests to study polymorphism in coagulation genes

Discussion

During the first month of life, the likelihood of thrombotic complications is 40 times higher than that at any other pediatric age, especially in critically-ill neonates or those who have a central catheter in place. In 18.6% of asymptomatic neonates, the prothrombin gene mutations are present. Mutation of factor V Leiden was identified as a vein thrombosis risk factor. Inherited thrombophilic disorders contribute to the development of thrombosis in children (9). Maturation of *PAI-1* and *MTHFR A1298C* coagulation genes was seen in our patient. The *MTHFR A1298C* homozygote mutation lowers the levels of functional enzyme resulting in higher levels of homocysteine, but to a lesser extent than the case of the homozygote *C677T* polymorphism.

Other than genetic and hereditary factors, catheterization is the most important risk factor for both arterial and venous thromboembolism. Approximately 90% of thromboembolic events are catheter-related (10). The presence of a catheter favors the occurrence of thrombosis by different mechanisms. Catheters may cause mechanical damage to the vascular wall and slow down or interrupt the blood flow (9). Argyle polyvinyl catheters and polyvinyl chloride catheters were found to be associated with increased thrombogenicity (11). It has been reported that 1% of newborns with catheters have symptoms indicative of thrombosis (12), and it is estimated that the incidence of catheter-associated asymptomatic thrombosis is 20-30% (13). Except for catheterization, asphyxia, septicemia, dehydration, and maternal diabetes have been mentioned as risk factors for neonatal thrombosis (1).

Cleft lip and/or palate is the most common congenital craniofacial anomaly (14). Cleft (opening) can occur on one (unilateral) or both sides (bilateral) with various ranges of severity. It can be difficult to feed babies with enough nutritious food when they have this condition, and there is evidence of delayed development in children born with a cleft (8). In our case, in addition to genetic maturation, cleft palate, and the following maternal lactation failure, dehydration and hypernatremia were the other underlying factors for thrombosis. In fact, in addition to the risk factors for thrombosis, which in our baby were hypernatremic dehydration and PICC, the severity and extent of thrombosis were largely due to her thrombophilia as an underlying disorder.

The diagnostic method of choice for thromboembolism is transthoracic echocardiography. Its most serious complication is pulmonary thromboembolism, which becomes apparent due to acute respiratory distress and stroke (9). Treatment alternatives include clinical observation, anticoagulation, thrombolytic therapy (systemic and catheter-directed), and surgical thrombectomy (15) .Our case experienced severe respiratory distress and immediately underwent surgery for thrombosis removal that requires high accuracy and excellence.

Conclusion

Our patient had various underlying conditions for the occurrence of thromboembolism. In a routine echocardiography assessment performed to exclude the possibility of heart problems, thrombosis was accidentally observed while it had no symptoms. Therefore, it is suggested to monitor neonates with these risk factors for thrombosis. On the other hand, checking poorly fed infants due to any reasons, including cleft palate, for hypernatraemic dehydration and the consequent thrombosis is important.

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Conflicts of interests

The Authors declare that there is no conflict of interest.

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